Purpura Following Treatment With Tetraethylammonium Chloride

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THE purpose of this article is to report a case of thrombocytopenic purpura resulting from the parenteral administration of tetraethylammonium chloride *(Etamon,* Parke, Davis and Co.).

Although the toxic effects of tetraethylammonium chloride or bromide on laboratory animals have been studied extensively,[1,2,3] no allergic manifestations or ill effects upon the blood have been reported. Since the first use of the drug in man by Lyons and his associates[5] there have been several studies in human beings,[4,6] none of which mention thrombocytopenic purpura as a possible complication of this treatment.

CASE REPORT

A white woman, aged 26 years, suffered a simple fracture of the right tibia with separation of the internal malleolus, on Feb. 9, 1946. The fractured limb was immobilized in a plaster cast for six months. After removal of the cast, the extremity appeared to be improving until about six months later (one year following the original injury), when it gradually became swollen, painful, cold, and extremely sensitive to touch. These symptoms persisted and grew progressively worse under conservative management elsewhere.

At the time of initial examination by the author, the right ankle was found to be swollen, mottled purple in color, exquisitely painful, moist to touch, cold, and with areas of hypesthesia and hyperesthesia not characteristic of peripheral nerve distribution. Roentgenographic examination showed a complete separation of the internal malleolus as a pseudarthrosis following the old fracture.

Operation was performed July 14, 1947, when the fractured malleolus was fixed in satisfactory position by means of a metallic screw. The cast was removed Aug. 11, 1947, and the patient instructed to bear weight on the foot on Sept. 2.

On Oct. 6, three months following operation, the patient complained of an exacerbation of the symptoms mentioned previously. The area was examined and the former findings confirmed. A diagnosis of reflex sympathetic dystrophy was made and a treatment program consisting of alternate hot and cold leg baths, massage, and Buerger's exercises twice daily was begun. One week later there had been no improvement and it was decided to use Etamon. Accordingly on Oct. 13, 14, 17 and 20 the patient was given a dose of 20 mg. per kg. of body weight (in each buttock 7 cc. of an aqueous solution containing 0.1 gm. of Etamon Chloride in each cc.). After these injections the swelling was dramatically relieved, the ankle was warm, bounding pulses were palpable, and the discoloration had disappeared.

On Nov. 23 the patient complained that the previous symptoms were recurring, although they were considerably milder than formerly. Another intramuscular injection of Etamon was given in the same dosage used in October. On Nov. 26 a purpuric eruption of the back developed without accompanying symptoms or evidence of bleeding elsewhere. A platelet count showed 99,220 per cubic mm. of blood. A second count on Nov. 26 showed 86,000 and a third on Nov 27 showed 91,005. The rash lasted about 72 hours and disappeared spontaneously. A platelet count on Dec. 11 was 161,000 and on Dec. 22 was 250,000.

A review of the history disclosed no other possible causative agent—the patient had taken no medicines of any kind for seven weeks preceding the first series of injections and for 11 weeks preceding the final one. There was no history of abnormal bleeding in the past and no history of personal or familial allergy. With the exception of the platelets, the constituents of the blood were normal on repeated examinations. There was no splenomegaly. Capillary fragility was not increased. Unfortunately, platelet counts were not made before the onset of purpura, but routine blood smears on July 14 and Oct. 10, 1947, were reported to show, respectively, that "platelets appear normal," and "platelets appear normal both numerically and morphologically."

It seems probable that this episode represents an allergic reaction to tetraethylammonium chloride characterized by a purpuric rash and an accompanying thrombocytopenia with spontaneous recovery.

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Streptomycin in Cryptococcosis

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THERE is still no known treatment of value in cases of torula meningitis. Shapiro and Neal[7] tried many therapeutic agents before the advent of sulfonamides and the antibiotics. They found none which in therapeutic doses would inhibit the growth of torula organisms. Others since then have been equally unsuccessful. Sulfonamides as well as penicillin have been tried in a few cases.[2,4,5,8] However, in only one case[4] has there seemed to be indication that sulfonamides were of help, and no observers seem to have indicated penicillin as being of any aid.

Tests in vitro with sulfonamides and penicillin have shown no inhibition of growth activity of the organism, and these agents have not prolonged the life of mice injected with torula.[3,8] Dawson and his co-workers list cryptococcus hominis as sensitive to penicillin. Robinson[6] found the organism insensitive in vitro to concentrations of 4,000 units of streptomycin and 250 units of streptothricin per cubic centimeter. In our own experience streptomycin in concentration of 25,000 micrograms per cc. has no inhibitory effect on in vitro growth of two strains of this organism tested.

Several factors make the trial of therapeutic agents difficult. There are at least 40 strains of torula organisms, eight of which are pathogenic. In addition, torulosis is infrequent. Voyles and Beck[8] in 1946 found 108 cases reported in the literature. In 54 of these only the central nervous system was involved. One rarely has a chance to treat a case of torulosis. Hence, only after a series of individual case reports can the value of a therapeutic agent be determined. The following, to the best of our knowledge, is the first case in which streptomycin has been used. This agent, and others, produced no noticeable effect on the outcome of the disease.

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